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TITLE: Hyperbaric Oxygen Therapy in the Treatment of Chronic Mild-Moderate Blast-Induced Traumatic Brain Injury PCS and PTSD

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of the study is to see if an eight-week course of forty low-pressure HBOT's can significantly improve symptoms and cognitive function in military veterans and civilians with mild TBI/PPCS. The proposed design is a randomized controlled (non-treatment, non-sham) single-arm crossover single-blind study. The scope of the project is to recruit, enroll, test, treat, re-test and follow-up on 50 subjects at Louisiana State University, New Orleans in 23 months and another 50 subjects at Oklahoma State University in an equivalent period of time. The study received final approval from all regulatory agencies on 5/13/2014. Enrollment began shortly thereafter. Thus far seven subjects have been enrolled. One enrolled subject defaulted on treatment due to urgent personal commitments at the time of enrollment. The other six are proceeding through the protocol. Three additional subjects have passed nearly all screening measures and will be undergoing the final screening and enrollment in the next 3 weeks. There are no study results to report at this time and no significant adverse advents.

15. SUBJECT TERMS

HBOT: hyperbaric oxygen therapy; TBI: traumatic brain injury; PPCS: persistent post-concussion syndrome

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ANNUAL REPORT

I. INTRODUCTION

Mild-moderate blast-induced traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) affect 11-28% and 13-17%, respectively, of U.S. combat troops returning from Iraq and Afghanistan. Mild TBI affects another 2 million civilians in the United States and far greater numbers worldwide. Approximately 10-15% of mild TBI patients experience the persistent post-concussion syndrome (PPCS). Evidence-based medicine exists for PTSD, but there is no effective treatment for the persistent post-concussion syndrome (PPCS) of mild-moderate TBI nor the combined diagnoses of PPCS and PTSD. Between the Fall of 2008 and end of 2010, the P.I. conducted a non-controlled pilot trial of hyperbaric oxygen therapy (HBOT 1.5 atmospheres absolute/60 minutes, twice/day, 40 treatments in one month) in military veterans with both TBI/PPCS and PTSD that achieved substantial symptomatic, cognitive, and brain imaging improvements in the subjects. Preliminary results were published 11/2011 in the Journal of Neurotrauma (http://www.liebertonline.com/doi/abs/10.1089/neu.2011 .1895). The original purpose of the present study was to replicate the pilot trial in a randomized sham-controlled double-blind design with the sham-control group receiving slightly pressurized air at the beginning and end of each treatment. After further review of the science and discussion with the FDA the study was changed to: 1) a randomized controlled (non-treatment non-sham) single-arm crossover single-blind design, 2) include both military and civilian subjects with the single diagnosis of PPCS from either blast or blunt trauma, and 3) an eight week course of treatment, instead of four weeks.

Therefore, the purpose of the new proposed study is to see if an eight-week course of forty low-pressure HBOT's can significantly improve symptoms and cognitive function in military veterans and civilians with mild TBI/PPCS using a randomized controlled single-arm crossover design. The scope of the project is to recruit, enroll, treat, test, retest, and follow-up test 50 subjects within 23 months at LSU, New Orleans and another 50 subjects at Oklahoma State University Health Sciences Center, Tulsa, Oklahoma.

II. BODY

The research accomplishments associated with the tasks in the Statement of Work of 12/18/2013 are as follows:

A. Obtain TATRC IRB and scientific reviews/approvals: IRB approval was obtained from LSU School of Medicine 12/18/2013. Second level (final) ORP approval was obtained on 5/13/2014. VA IRB submission was planned after ORP approval, but abandoned due to the high probability of inestimable

further delays. In the previous 4 years the P.I. had experienced significant delays in obtaining research privileges at the VA, been unable to obtain written confirmation of privileges, received misinformation on the necessity of credentialing a previous VA employee co-investigator, proceeded to obtain privileges for the co-investigator, and then was informed of a purported loss of co-investigator's electronic Vet-Pro application six months after submission. Given this pattern of events and the unlikelihood of credentialing of the co-investigator in a reasonable period of time, if at all, the P.I. felt the eventual execution of the study was in jeopardy and elected to proceed without VA IRB approval.

B. Recruit sufficient numbers of appropriate subjects to complete the study within project period: The rapid approval by ORP was followed by local CBS television airing in early June. Granting of a No Cost Extension allowed relaxation of a very optimistic recruitment expectation in the Year 4 First Quarter Report (April, 2014). Recruitment proceeded through the end of August on target, during which time email, phone advertising and announcement, website posting, and contact with all sources mentioned in the 12/18/2013 SOW occurred. Despite this effort enrollment slowed in late August and early September. Billboard posting and direct mailing ensued. We are averaging approximately 15 calls/week and have enrolled seven subjects. The first subject was enrolled on 8/8/2014. One enrolled subject defaulted on treatment due to urgent personal commitments at the time of enrollment. The other six are proceeding through the protocol. Three additional subjects have passed nearly all screening measures and will be undergoing the final screening and examination in the next 3 weeks. Since the first enrolled subject we have averaged 2-3 enrolled subjects/month. At the present pace we will need the full length of the study to recruit all 50 subjects unless there is accelerated recruitment of veterans through the VA. We intend additional advertising efforts and are appealing to outside VA hospitals and programs. Thus far, we have had no referrals from the local VA community.

C. Enroll, test, and treat 50 subjects within 17 months from award date: Based on the final ORP approval date of 5/13/2014 and the NCE which extends the study through March 30, 2016 the timeline to enroll, test, treat, and follow-up retest subjects should be extended to 23 months after ORP approval, the formal starting date of the study. Tasks 3.a.-f. in the SOW have not changed. Each subject is adhering to this schedule. They are renumbered C.1-6 with appropriate change of dates:

1. Recruit subjects, beginning the end of May, 2014. Patients in the HBOT Group will complete the protocol in 18 weeks while patients in the Control Group will complete the protocol in 27 weeks.

2. Obtain consent, take hyperbaric medicine history, and conduct physical exam at the hyperbaric facility (Family Physicians Center) and

additional study site. This subtask will be completed during the week of recruitment, most likely on the day the subject is recruited.

3. Perform psychometric testing and questionnaires at Neuro-psychological and Psychological Services for Children and Adults, LLC, 2626 N. Arnoult Rd, Ste 220, Metairie, LA, which is 10 miles from the hyper-baric facility. The collaborator performing this task is Dr. Susan Andrews. This task will be accomplished during the first week of recruitment, most likely on the second day. The same task will be completed at the second study site on the same timeline.

4. Post-treatment physical exam conducted by the PI at the hyperbaric facility on or about the day of the 40th hyperbaric treatment.

5. Repeat psychometric testing and questionnaire completion by Dr. Andrews the day following the 40th hyperbaric treatment.

6. Repeat NSI and QOLIBRI eight weeks following the 40th hyperbaric treatment.

D. Analyze data and submit a manuscript for peer-reviewed publication within 24 months of funding: Given the timeline in C. a more accurate statement of this goal would be a publication within 31 months of first enrollment.

III. KEY RESEARCH ACCOMPLISHMENTS

The key research accomplishment is the beginning of the study and enrollment of 7 subjects without any significant adverse events.

IV. REPORTABLE OUTCOMES

There are no reportable outcomes since the study has just begun. No data has been analyzed.

V. CONCLUSION

The study has completed the regulatory phase and is actively recruiting. Seven subjects have been enrolled and six are proceeding through the protocol without significant adverse events.

VI. REFERENCES

There are no references.

VII. APPENDICES

There are no appendices.

VIII. SUPPORTING DATA

There is no supporting data.